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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/032,072	12/31/2001	Frank Man-Woon Ng	017227-0184	5966

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EXAMINER	
CELSA, BENNETT M	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 05/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/032,072	NG ET AL.	
	Examiner	Art Unit	
	Bennett Celsa	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-25* is/are pending in the application.

4a) Of the above claim(s) *23 and 24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-22 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/31/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

Claims 18-25 are currently pending.

Claims 23-24 are withdrawn from consideration.

Claims 18-22 and 25 are under consideration.

Election/Restrictions

1. Applicant's election with traverse of hGH 177-191 (seq. Id. 1) in the reply filed on 3/17/05 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

I. It is noted that the present application (10/032,072: filed 12/31/01) is a:

Continuation of 09/245,712 (filed 2/8/99: Patent 6,335,319) which is a

CIP of 08/340,389 (filed 11/15/94: Patent 5,869,452).

Present claim 18 (and claims 19-21 and 25 dependent thereon) contains new subject matter not disclosed in the 08/340,389 application e.g. a method of treating obesity comprising administering to a mammal in need thereof an effective amount of a peptide or homologue/analogue/mutant/variant or derivative thereof comprising a a carboxyl terminal sequence comprising *a bioactive lipid metabolic domain of growth hormone* effective to reduce body weight gain and adipose tissue mass in an obese mammal, which is not the intact, full length mammalian growth hormone exclusive of peptides comprising hGH 177-91 (or

corresponding mamamalian sequences). Accordingly, claims 18-21 and 25 are not afforded 35 USC 120 priority of he 11/15/94.

II. Claims 18-21 and 25 are denied 35 USC 120 priority for failure to satisfy 35 USC 112/1 for both enablement and written description as discussed below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 18-21 and 25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (LACK OF WRITTEN DESCRIPTION).

The presently claimed invention is directed to a method of treating mammalian obesity, comprising administering to a mammal in need thereof an effective amount of a peptide or a "homologue/analogue/mutant/variant/or derivative thereof' wherein:

a. the peptide comprises a "carboxyl-terminal sequence of a mammalian growth hormone comprising a 'bioactive lipid metabolic domain of the growth hormone' which is "not the intact, full-length mammalian growth hormone"; and wherein

b. the "homologue/analogue/mutant/variant/or derivative thereof" of the peptide retains the ability to reduce body weight gain and adipose tissue mass in an obese mammal.

The specification definition for "homologue/analogue/mutant/variant/or derivative thereof" is open, since it "may be defined" (but is not so limited) to encompass "insertion deletion or substitution of amino acids in, or chemical modification of, the native carboxyl-terminal sequence". Similary, although exemplified (e.g. acetylation of NH terminus and/or amidation of COOH terminus and/or side chain cyclisation of the native carboxyl-terminal sèquence) chemical modification is an open definition. Accordingly, a large number of "transformed" peptides of variable structure (and conformation?) are encompassed within the broad specification definition of the "homologue/analogue/mutant/variant/or derivative thereof" of claimed peptides.

Additionally, it is pointed out that the claims (e.g .claims 10-12 and 17) encompass peptide sequences which comprise bioactive lipid metabolic domain of growth hormone which is not the intact, full length mammalian growth hormone, exclusive of peptides comprising hGH 177-91.

The specification provides examples demonstrating the use of a specific peptide (e.g. hGH 177-191) for treating obesity in an animal model. The specification fails to provide a single example of a pharmaceucitically active peptide homologue/analogue /mutant/variant/or derivative thereof" that retains the ability to reduce body weight gain and adipose tissue mass in an obese mammal or any teaching as to what modifications (and where such modifications are made) in a mammalian GH which enable it to maintain its therapeutic obesity properties. Similarly, no evidence regarding bioactive lipid metabolic domains other that residues 177-191 is described.

It is first noted that written description is legally distinct from enablement: "Although the two concepts of are entwined, they are distinct and each is evaluated under separate legal criteria. The written description requirement, a question of fact, ensures the that the inventor conveys to others that he or she had possession of the claimed invention; whereas, the enablement requirement, a question of law, ensures that the inventor conveys to others how to make and use the claimed invention." See 1242 OG 169 (January 30, 2001) citing *University of California v. Eli Lilly & Co* With regard to the description requirement. The Court of Appeals for the Federal Circuit held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.,* 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)]. In this regard, applicant is further referred to "Guidelines for Examination of Patent Applications Under the 35 USC 112, first paragraph, 'Written Description' Requirement" published in 1242 OG 168-178 (January 30, 2001); *Enzo Biochem. Inc.v. Gen-Probe Inc.*, Case No. 01-1230 (Fed. Cir. July 15, 2002) ("EnzoII"); and Univ. Of Rochester v G. D. Searle and Co. 249 F. Supp. 2d 216 (W.D.N.Y. 2003) affirmed by the CAFC on February 13, 2004 (03-1304) 69 USPQ2d 1886. .

Accordingly, the specification showing of the the use of a specific peptide (e.g. hGH 177-191) for treating obesity in an animal model simply does not provide

adequate written description for pharmaceutically active peptide homologue/analogue /mutant/variant/or derivative thereof" that retains the ability to reduce body weight gain and adipose tissue mass in an obese mammal; nor does the specification showing of a single bioactive lipid metabolic domain of residues 177-191 provide adequate written description for a generic of such domains exclusive of the 177-191 sequence.

3. Claims 18-21 and 25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for pharmaceutical compositions comprising amino acid residues 177-191 hGH (or mammalian sequences corresponding thereto) to treat obesity in a mammal, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the present claims.

There are many factors to consider when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any experimentation is "undue". These factors include, but are not limited to:

a. The breadth of the claims.
b. The nature of the invention
c. The state of the prior art;
d. The level of one of ordinary skill
e. The level of predictability in the art;
f. The amount of direction provided by the inventor;
g. The presence or absence of working examples;
h. The quantity of experimentation necessary needed to make or use the invention based on the disclosure;

See :*In re Wands* USPQ 2d 1400 (CAFC 1988):

(1-2) ***The breadth of the claims and the nature of the invention:***

The presently claimed invention is broadly directed to a method of treating mammalian obesity, comprising administering to a mammal in need thereof an effective amount of a peptide or a "homologue/analogue/mutant/variant/or derivative thereof" wherein:

a. the peptide comprises a "carboxyl-terminal sequence of a mammalian growth hormone comprising a 'bioactive lipid metabolic domain of the growth homone' which is "not the intact, full-length mammalian growth hormone"; and wherein

b. the "homologue/analogue/mutant/variant/or derivative thereof" of the peptide retains the ability to reduce body weight gain and adipose tissue mass in an obese mammal.

The specification definition for "homologue/analogue/mutant/variant/or derivative thereof" is open, since they "may be defined" to encompass "insertion deletion or substitution of amino acids in, or chemical modification of, the native carboxyl-terminal sequence. Similary, although exemplified (e.g. acetylation of NH terminus and/or amidation of COOH terminus and/or side chain cyclisation of the native carboxyl-terminal sequence) chemical modification is similarly an open definition. Accordingly, a large number of "transformed" peptides of variable structure (and conformation?) are encompassed within the broad specification definition of "homologue/analogue/mutant/variant/or derivative thereof" of the peptide encompassed by the present claims.

Additionally, it is pointed out that the claims (e.g .claims 10-12 and 17) encompass peptide sequences which comprise bioactive lipid metabolic domain of growth hormone which is not the intact, full length mammalian growth hormone, exclusive of hGH 177-91.

(3 and 5) ***The state of the prior art and the level of predictability in the art:***

Regarding, the unpredictability in the GH related art the following is noteworthy. Human placental lactogen (hPL) which is highly homologous (.>80%) to human, bovine and chicken growth hormones completely lacks lipolytic or anti-lipolytic activity (See Campbell et al., Proc. Soc. Exper. Biol. Med. Vol. 193 no. 4 (4/90) pages 269-273 at 272).

Additionally, the effect of a single amino acid substitution of hGH and analogues thereof has been shown to result in a dramatic change in peptide conformation and adipogenic activity (e.g. see Nishikawa et al., Prot. Engin. Vol. 3 No. 1 (1989) pages 49-53 at page 52, left column). Accordingly, the affect on the bioactivity of derivatazing a given peptide is unpredictable.

It is also noted that the cellular and molecular action of the presently claimed peptides is unknown.

(4) ***The level of one of ordinary skill in the art:***

The level of skill would be high, most likely at the Ph.D. level.

(6-7) ***The amount of direction provided by the inventor and the existence of working examples.***

The specification provides examples demonstrating the use of a specific peptide (e.g. hGH 177-191) for treating obesity in an animal model. The specification fails to provide a single example of a pharmaceutically active peptide homologue/analogue /mutant/variant/or derivative thereof" that retains the ability to reduce body weight gain and adipose tissue mass in an obese mammal or any teaching as to what modifications (and where such modifications are made) in a mammalian GH which enable it to

maintain its therapeutic obesity properties. Similarly, no evidence regarding bioactive lipid metabolic domains other than residues 177-191 is described.

(8) ***The quantity of experimentation needed to make or use the invention based on the content of the disclosure:***

Due to the unpredictability of the GH related art; the lack of guidance regarding the amino acid sequences in growth hormones other than hGH and modification thereof which produce the related effect; the scope of the presently claimed invention; and the difficulty in extrapolating *in vitro* data to *in vivo* utility; the presently claimed invention is not enabled for its present scope. The specification has failed to provide adequate guidance to enable the skilled artisan to reliably extrapolate bioactivity realized by a specific human growth hormone peptide to other growth hormones which differ in sequence, specificity and chemical/physical and biological characteristics. Absent this commensurate showing, finding other peptide species with the desired efficacy would represent undue experimentation.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 18-21 and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 18 (and claims dependent thereon), the phrase "carboxyl-terminal sequence of a mammalian growth hormone" lacks metes

and bounds regarding what amino acid residues constitute the carboxy-terminal sequence of a given growth hormone to inform the public as to what infinges and what does not infringe the claim. For the specification fails to define what amino acids with respect to human growth hormone, as well as other mammalian species, would constitute a "carboxy terminal sequence". Thus, it is unclear as to where the amino terminus ends and a "carboxyl terminal sequence" begins.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 18-22 are rejected under 35 U.S.C. 102(a,b) as being anticipated by Natera et al. Biochem. & Mol. Biol. Int'l, Vol. 33 (5) (Aug 1994) pages 1011-1021) in view of the present specification and claims as evidence of inherency.

The presently claimed invention (e.g. claim 18) is drawn to a method of treating mammalian obesity, comprising administering to a mammal in need thereof an effective amount of a peptide or a "homologue/analogue/mutant/variant/or derivative thereof" wherein:

a. the peptide comprises a "carboxyl-terminal sequence of a mammalian growth hormone comprising a 'bioactive lipid metabolic domain of the growth homone' which is "not the intact, full-length mammalian growth hormone"; and wherein

b. the "homologue/analogue/mutant/variant/or derivative thereof" of the peptide retains the ability to reduce body weight gain and adipose tissue mass in an obese mammal.

Natera et al. teach pharmaceutical compositions that reduce cumulative body weight gain and decrease adipose tissue mass, comprising hGH 177-191 which are intraperitoneally injected into mice (e.g. comprising "one or more pharmaceutically

acceptable carriers and/or diluents") in amounts within the scope of the presently claimed invention (e.g. 200 ugms/kg is within the scope of amounts disclosed as "an effective amount of a peptide"). The reference hGH 177-191 peptide MUST INHERENTLY comprise:

a "carboxyl-terminal sequence of a mammalian growth hormone comprising a 'bioactive lipid metabolic domain of the growth hormone' which is "not the intact, full-length mammalian growth hormone" and

b. lacks the diabetogenic property of the intact, full length mammalian growth hormone, since the reference peptide reads on the peptide of present claim 22 and lacks the amino terminal portion disclosed in the specification to be responsible for insulin-like action (e.g. diabetogenic) of hGH .

7. Claims 18-21 and 25 are rejected under 35 U.S.C. 102(a,b,e) as being anticipated or alternatively prima facie obvious over Clark, U.S. Pat. No. 5,597,797 (1/97: 102e date: 11/19/93) and the specification as evidence of inherency taken alone or further in view of Seeburg, US Pat. No. 4,670,393 (6/87), Wells et al. WO 90/04788 (5/90) or Garrard WO 92/09690 (6/92).

The presently claimed invention (e.g. claim 18) is drawn to a method of treating mammalian obesity, comprising administering to a mammal in need thereof an effective amount of a peptide or a "homologue/analogue/mutant/variant/or derivative thereof" wherein:

a. the peptide comprises a "carboxyl-terminal sequence of a mammalian growth hormone comprising a 'bioactive lipid metabolic domain of the growth hormone' which is **"not the intact, full-length mammalian growth hormone"**; and wherein

b. the "homologue/analogue/mutant/variant/or derivative thereof" of the peptide retains the ability to reduce body weight gain and adipose tissue mass in an obese mammal.

Present claim 19, further requires that the peptide "does not have the diabetogenic property of the **intact, full-length** mammalian growth hormone. In this respect, the specification teaches that GH (e.g. hGH) proteins which lack their amino terminal portion (e.g. @ 1st 50 amino acids) would inherently meet the claim 19 limitation, since the NH terminal portion of hGH is disclosed in the specification to be responsible for the insulin-like action (e.g. diabetogenic) of hGH .

Clark discloses (e.g. see col. 2-3) and claims the use of "GH" (including hGH as well as corresponding peptides from various species including bovine, ovine, porcine, equine: see col. 8, lines 12-15) alone (e.g. see patent claim 18 and examples) or in combination with IGF-I to treat obesity utilizing pharmaceutical formulations including oral delivery dosage forms (e.g. See Abstract; columns 9 and 13-15; the Examples; patent claim 12). Clark teaches that the making of pharmaceutical growth formulations (e.g. bioactive amounts and types of pharmaceutical diluents/carriers) for oral, as well as other modes of administration (e.g. parenteral, including injectables) for administration to mammals is well within the skill of the art. E.g. see Clark, col. 9-17. For example, Clark teaches "sustained-release" systems for oral administration of GH. E.g. see col. 13-14.

The Clark reference defines "GH" (e.g see col. 8) to encompass:

a. human native sequence GH (e.g. "intact, full length mammalian growth hormone");

b. met-hGH ; and

c. "GH variants" 'as described in US Pat. No. 4,670,393 ... WO 90/04788 ... and WO 92/09690 published 11 Jun. 1992'. See col. 8, lines 18-43.

It is noted that the use of a generic of GH variants alone or in combination with IGF would constitute both peptides and compositions within the scope of the presently claimed invention since the GH variants AND met-hGH are necessarily NOT full-length INTACT mammalian growth hormones and applicant's claims are not limited to the administration of GH alone in view of open ended "comprising" terminology.

Alternatively, the selection of met-hGH or GH variants as disclosed in the Seeburg US Pat. No. 4,670,393 (6/87), Wells et al WO 90/04788 (5/90) or Garrard WO 92/09690 (6/92) for treating obesity is suggested by the Clark reference at col. 8. Accordingly, the selection of GH variants from these references would have been immediately envisaged (e.g. anticipated) , or in the alternative prima facie obvious since the Clark reference uses GH or met-hGH or GH variants alternatively. See *In re Schaumann*, 197 USPQ 5 (CCPA 1978)

With respect to reference GH variants disclosed in the Seeburg US Pat. No. 4,670,393 (6/87), Wells et al WO 90/04788 (5/90) or Garrard WO 92/09690, such variants are exemplified as follows: see Seeburg col. 3 and patent claims including claim 1. See Wells at Abstract (e.g. last sentence); page 6, lines 8-12; page 17, lines

10-12; page 41; page 42, lines 1-10; page 49, lines 22-35; page 62, lines 8-22; claims 32-83; Fig. 29. See Garrard et al. at page 20, lines 5-15, lines 33-38; Tables I-XVI; and claims drawn to GH variants e.g. claims 24, 39, 40, 48 etc..

To the extent that the GH variants suggested by the Clark reference and exemplified by the Seeburg, Wells and Garrard reference "comprise" mammalian carboxy terminal GH sequences (e.g. residues "corresponding" to 177-191) which are NOT " INTACT full length mammalian growth hormone" such GH variants must meet explicitly or inherently the presently claimed invention e.g. possess "a bioactive lipid metabolic domain of the GH" effective to reduce body weight gain and adipose tissue mass in obese mammals and thus anticipate claims 10, 12, 13 and 17. See *In re Best*, 195 USPQ 430,433 (CCPA 1977); *Ex parte Novitski*, 26 USPQ2d 1389 (B.P.A.I, 1993); See also present specification and claims as providing evidence of such properties being inherent in the reference peptides.

Accordingly, the Clark reference, taken separately, or in combination with Seeburg, Wells or Garrart would anticipate, or in the alternative, render obvious the use of met-hGH or other GH variants in sustained release formulations (e.g. oral) for treating obesity thus anticipating or rendering obvious claims 10, 12, 13 and 17.

Regarding claim 19 and the limitation that "the peptide not have the diabetogenic property of the intact, full length mammalian growth hormone", GH variant peptides disclosed and claimed in the Wells reference (E.g. see claims 32-64, especially claims 34, 38-41, 53-56, 59-64) which substitute/insert/delete within the N-terminal portion of GH would be expected to "inherently" lack "the diabetogenic property of the intact, full

length mammalian growth hormone" since disruption of the core sequence would be expected to destroy receptor binding necessary to effect such activity. The PTO lacks experimental facilities to make comparisons of prior art compound (s).

8. Claims 18-22 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natera et al. Biochem. & Mol. Biol. Int'l, Vol. 33 (5) (Aug 1994) pages 1011-1021) {and use of specification evidence of inherency} and Clark, U.S. Pat. No. 5,597,797 (1/97: 102e date: 11/19/93).

The presently claimed invention (e.g. claim 18) is drawn to a method of treating mammalian obesity, comprising administering to a mammal in need thereof an effective amount of a peptide or a "homologue/analogue/mutant/variant/or derivative thereof" wherein:

a. the peptide comprises a "carboxyl-terminal sequence of a mammalian growth hormone comprising a 'bioactive lipid metabolic domain of the growth hormone' which is **"not the intact, full-length mammalian growth hormone";** and wherein

b. the "homologue/analogue/mutant/variant/or derivative thereof" of the peptide retains the ability to reduce body weight gain and adipose tissue mass in an obese mammal.

Present claim 19, further requires that the peptide "does not have the diabetogenic property of the **intact, full-length** mammalian growth hormone. In this respect, the specification teaches that GH (e.g. hGH) proteins which lack their amino terminal portion (e.g. @ 1st 50 amino acids) would inherently meet the claim 19 limitation, since the NH terminal portion of hGH is disclosed in the specification to be responsible for the insulin-like action (e.g. diabetogenic) of hGH .

Natera et al. teach pharmaceutical compositions that, reduce cumulative body weight gain and decrease adipose tissue mass, comprising hGH 177-191 which are intraperitoneally injected into mice (e.g. comprising "one or more pharmaceutically acceptable carriers and/or diluents") in amounts within the scope of the presently claimed invention (e.g. 200 ugms/kg is within the scope of amounts disclosed as "an effective amount of a peptide").

The Natera hGH 177-191 peptides MUST INHERENTLY comprise:

a "carboxyl-terminal sequence of a mammalian growth hormone comprising a 'bioactive lipid metabolic domain of the growth hormone' which is "not the intact, full-length mammalian growth hormone" and

b. lack the diabetogenic property of the intact, full length mammalian growth hormone since the reference peptides read on the peptide of present claim 19 and lack the amino terminal portion disclosed in the specification to be responsible for the insulin-like action (e.g. diabetogenic) of hGH .

The Natera pharmaceutical compositions comprising hGH177-191 differ from the presently claimed invention (e.g. claim 25) by failing to teach oral administration. .

However, the Clark reference teaches that the making of pharmaceutical growth formulations (e.g. bioactive amounts and types of pharmaceutical diluents/carriers) for oral, as well as other modes of administration (e.g. parenteral, including injectables) to mammals is well within the skill of the art. E.g. see Clark, col. 9-17. For example, Clark teaches "sustained-release" systems for oral administration of GH. E.g. see col. 13-14.

One of ordinary skill in the art would be motivated to formulate oral pharmaceutical formulations of the Natera peptides for mammalian delivery (e.g. mouse/rat/human) in order to determine whether the resulting orally administratable pharmaceutical compositions possess analogous bioactivity compared to the reference pharmaceutical compositions administered by mammalian injection.

Accordingly, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of applicant's invention to formulate analogous orally administratable pharmaceutical compositions to the injectable pharmaceutical compositions disclosed in the Natera references in order to evaluate/compare the resulting biological activity of the hGH177-191 peptide.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 19-22 and 25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 5,869,452. Although the conflicting claims are not identical, they are not

patentably distinct from each other because the patented claims disclose the therapeutic use (E.g. treating mammalian i.e. animal obesity) of a peptide (e.g. consisting essentially of hGH 177-191) within the scope of the presently claimed invention wherein and thus the patented peptide must:

a. comprise a "carboxyl-terminal sequence of a mammalian growth hormone comprising a 'bioactive lipid metabolic domain of the growth hormone' which is "not the intact, full-length mammalian growth hormone" and lack the diabetogenic property of the intact, full-length mammalian growth hormone (present claim 19).; and upon administration "inherently"

b. reduce body weight gain and adipose tissue mass in an obese mammal.

11. Claims 19-22 and 25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6,335,319. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims disclose the therapeutic use (E.g. treating mammalian i.e. animal obesity) of a peptide (e.g. consisting essentially of hGH 177-191) which comprises a "carboxyl-terminal sequence of a mammalian (e.g. human) growth hormone comprising a 'bioactive lipid metabolic domain of the growth hormone' which is "not the intact, full-length mammalian growth hormone" and lack the diabetogenic property of the intact, full-length mammalian growth hormone (present claim 19).; and upon administration reduces body weight gain and adipose tissue mass in an obese mammal.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bennett Celsa whose telephone number is 571-272-0807. The examiner can normally be reached on 8-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bennett Celsa
Primary Examiner
Art Unit 1639

BC
May 16, 2005